Armed Forces College of Medicine

AFCM

Heart failure (1)

By

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

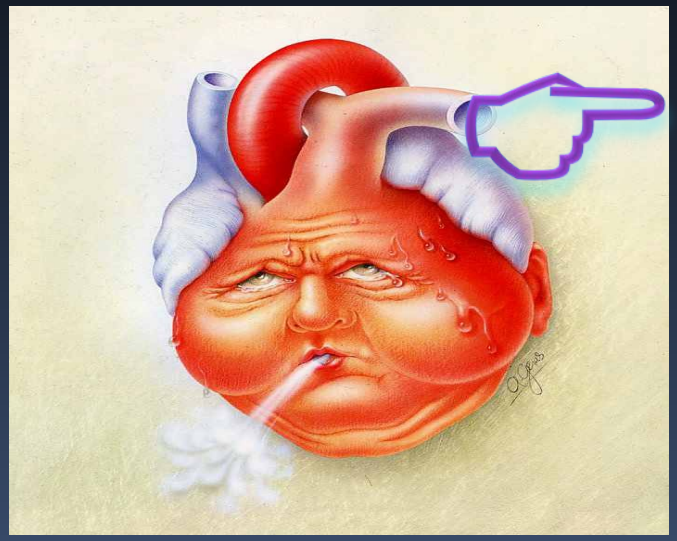
1.Identify the drugs used in treatment of heart failure

2.Explain the mechanism of action of different drugs used in treatment of heart failure

3.Describe the adverse effects of different drugs used in treatment of heart failure

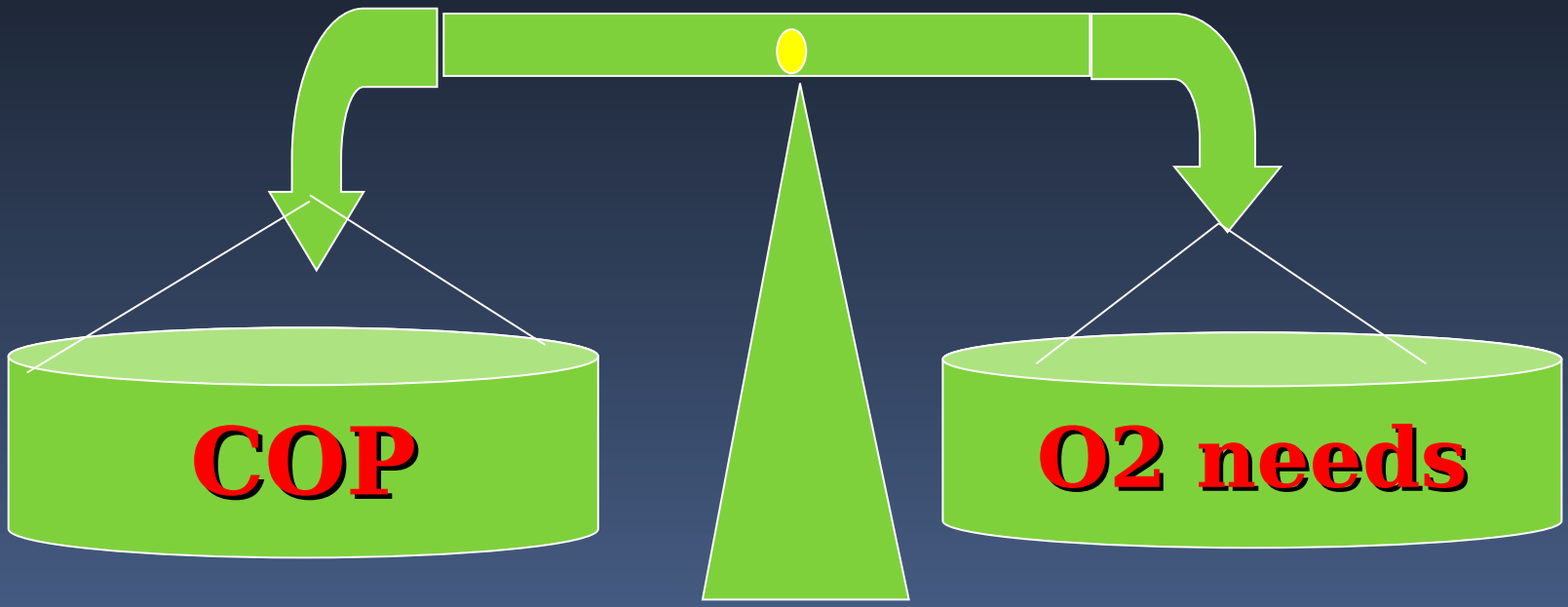
HEART FAILURE

Heart Failure



⇩ C.O.P

♥ **Heart failure is a life-threatening condition in which the heart can no longer pump enough blood**


COP
O2 needs

Classification of heart failure

Duration

Acute heart failure (AHF)
Chronic heart failure (CHF)

Side of heart affected

Left sided HF
Right sided HF

Pathophysiology of heart failure

Cardiac remodeling:

1. Hypertrophy

⇩ C.O.P

2. ↑Sympathetic activity:
   - ↑ H.R.
   - V.C

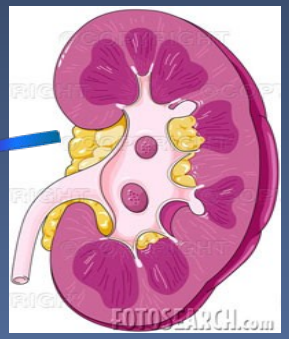
⇩

∀↑ E.D.V

↑Pre-load.

↑After-load

Angiotensin



Aldosterone

⇦ Na⁺ & water retention

Treatment of heart failure

β-blockers

⇩ C.O.P

1. Hypertrophy & Dilatation

⇩

∀↑ E.D.V

Positive Inotropics

2. ↑Sympathetic activity:

- H.R.
- V.C

↑Pre-load.

↑After-load

Venular vasodilators

Arteriolar vasodilators

ARBs

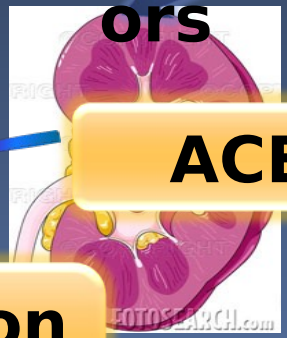
ACE-I

Diuretics

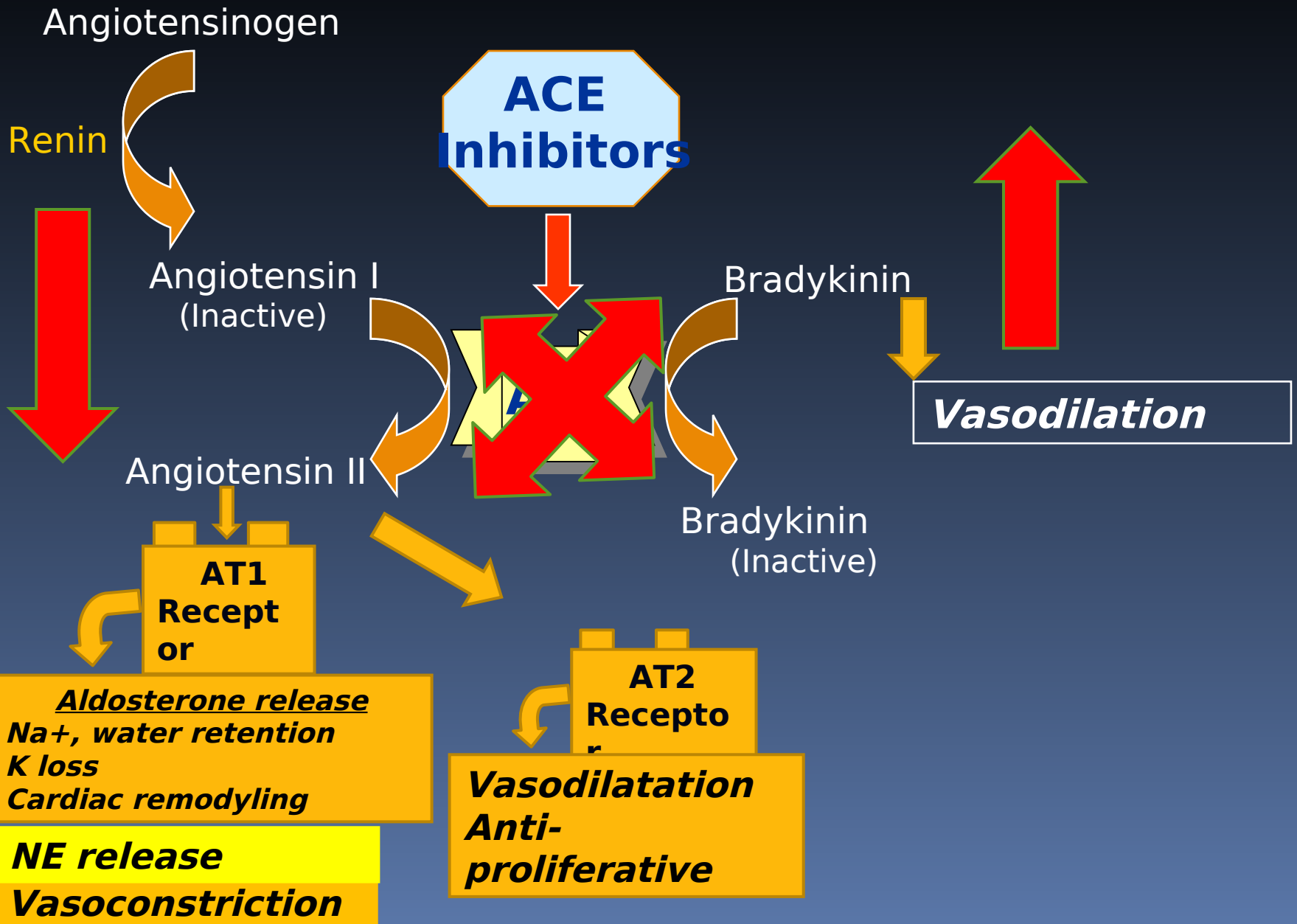
Na⁺ & water retention

⇦

Spironolactone & Eplerenone

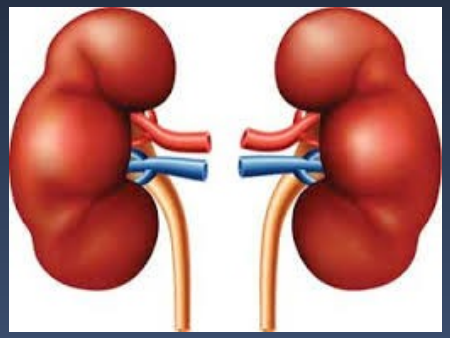


Angiotensin-Converting Enzyme Inhibitors (ACEIs)


Angiotensinogen
Renin
ACE Inhibitors
Angiotensin I
(Inactive)
Bradykinin
Vasodilation
Angiotensin II
Bradykinin
(Inactive)
AT1 Recept or
Aldosterone release
Na+, water retention
K loss
Cardiac remodyling
NE release
Vasoconstriction
AT2 Recepto r
Vasodilatation
Anti-proliferative

Advantages of ACEIs

-Renoprotective especially in diabetics.



-Do not induce reflex tachycardia, salt & water retention

Members of ACEIs:

Captopril: 1st ACEI, short acting ($t_{½}$ < 2 h) → taken 3 times/day (not a prodrug).

Enalapril – Perindopril - Ramipril - Lisinopril - Fosinopril

All (except lisinopril) are prodrugs requiring activation in liver.

Long duration (given once/day).

Lisinopril may be given in liver disease (no hepatic metabolism).

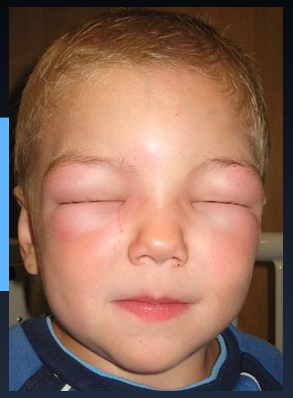
Fosinopril is highly lipid soluble with dual elimination; hepatic & renal→ no need for dose adjustment in renal disease. It may have a greater effect on tissue ACE in the heart.

Enalaprilat: active metabolite of enalapril. The only ACEI given IV→ used in emergency.

Adverse

MOST COMMON
Chronic dry cough

MOST SERIOUS
Angioedema

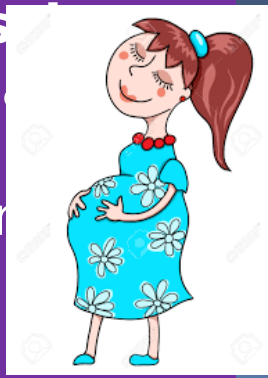


LESS COMMON

1-1st dose hypotension
2-Hyperkalemia:
3-- **Hypersensitivity:**
4- GIT:
- Anorexia- vomiting.
- Taste disturbance.
- Diarrhea.

SERIOUS
1-Renal impairment (reversible):
More common in **high renin states**:
a. Patients on diuretics
b. Bilateral renal artery stenosis

2-Bone marrow depres
3-Fetotoxic: if given in l
trimester.
4-Teratogenic if given i
trimester.



. Angiotensin II Receptor Blockers (ARBs)

Members:

Old: Valsartan - Losartan.

New: Candesartan – Irbesartan - Eprosartan - Telmisartan.

Mechanism of action:

Block AT_1 receptor which mediates most of the pathological cardiovascular effects of Ag II.

Spare AT_2 receptor → vasodilation & anti-proliferative effects.

Disadvantages compared to ACEIs

Lack of vasodilator effects of BK.

Advantages over ACEIs

1-No BK production→ no cough (angioedema still occurs).

2-↑Activity of AgII at AT2 receptor →↑VD & antiproliferative effects.

DIURETICS

Loop Diuretics: 1st choice especially in refractory or pulmonary edema (IVI).

Thiazides: may be added in refractoriness to loop diuretics.

Spironolactone:

a- added to loop diuretics & ACEIs→↓ mortality by 30%, by antagonizing systemic & local effects of excess aldosterone resulting in:

a. ↓ Na^+ retention and worsening of edema.

b. Minimize diuretic- induced hypokalemia →↓ arrhythmia & sudden death.

c. ↓ Myocardial hypertrophy & fibrosis induced by local aldosterone.

Beta Blockers

Carvedilol, bisoprolol & metoprolol

- decrease mortality by 30% when added to ACEIs & diuretics in hemodynamically stable patients.

-lock the **Sympathetic and Renin angiotensin system** activation in HF.

Beneficial effects in HF

1. ↓ HR → ↑ coronary flow.
2. ↓ Afterload and ↓ O_2 demand.
3. Cardioprotection: block catecholamine & Ag II - induced arrhythmia, myocardial damage & apoptosis.
4. Improve LV remodeling.
5. Resensitize the downregulated b_1 receptors (in long standing HF) → improve cardiac contractility

Lecture quiz

- **Which of the following is a common adverse effect of ACEI?**

A. Hypokalemia

B. Hyperglycemia

C. Cough

D. Constipation

E. Salt and water retention

Lecture quiz

- Which of the following drug is highly effective in treatment of pulmonary edema due to heart failure?

a. Loop diuretics

b. Beta blockers

c. Thiazide diuretics

d. Angiotensin receptor blockers

e. Calcium channel blockers

Lecture quiz

β-Blockers improve cardiac function in HF by?

A. decreasing cardiac remodeling

B. increasing heart rate

C. increasing renin release

D. activating norepinephrine

E. Improve myocardial contractility

SUGGESTED TEXTBOOKS

1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer

2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.

Thank You